

REMARKS

The presently claimed invention features isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence that is at least 80% identical to the amino acid sequence of SEQ ID NO:2 and has phosphoglycerate mutase activity.

SEQ ID NO:2 is the sequence amino acid sequence of an *M. incognitapphosphoglycerate mutase*.

Objections to the Specification

Applicants have amended the specification in response to objections made by the Examiner.

Objections to the Claims

The Examiner state the claim 4 improperly depended from claim 4, which has been cancelled. Applicants believe that the Examiner meant to state that claim 8 improperly depended from claim 4. Claim 8 has been cancelled.

Rejections Under 35 U.S.C. §112, second paragraph

The Examiner rejected claim 8 as indefinite for referring to SEQ ID NO:3 as a nucleotide sequence. Claim 8 has been amended to refer to the open reading frame of SEQ ID NO:1. This amendment is supported by the specification, for example, at lines 27-29 of page 15. No new matter has been added.

Rejections Under 35 U.S.C. §112, first paragraph (written description)

The Examiner rejected claims 5, 6, 8 and 10 as allegedly failing to meet the written description requirement of 35 U.S.C. §112, first paragraph.

The Examiner stated that the claims do not state the function of the polypeptides encoded by the claimed genus of nucleic acid molecules. Claim 8 has been amended to specify that the

encoded polypeptide has phosphoglycerate mutase activity. Thus, present claim 8 is drawn to a purified polypeptide that: 1) comprises an amino acid sequence that is at least 80% identical to SEQ ID NO:2 (an *M. incognita* phosphoglycerate mutase); and 2) has phosphoglycerate mutase activity. Phosphoglycerate mutase (PGM) is an enzyme of the glycolytic and gluconeogenic pathways that catalyzes the interconversion of 3-phospho-D-glycerate [3-PGA] and 2-phospho-D-glycerate [2-PGA] in the Embden-Meyerhoff pathway. The present specification provides a detailed description of an *in vitro* assay that can be used to assess the ability of a polypeptide to catalyze the conversion of oxaloacetate to malate (see page 36 of the specification). The specification provides an assay for measuring phosphoglycerate mutase activity, see, e.g., page 40. Those of ordinary skill in the art know other such assays. Thus, those skilled in the art can determine whether a polypeptide, e.g., a polypeptide that comprises an amino acid sequence that is least 80% identical to SEQ ID NO:2 has phosphoglycerate mutase activity.

In *Regents of the University of California v. Eli Lilly & Co.*, the Court of Appeals for Federal Circuit held that an adequate written description of genetic material “requires a precise definition, such as by structure, formula, chemical name, or physical properties.” 119 F.3d at 1563. The presently claimed nucleic acid molecules are defined by sequence or by sequence combined with function. Thus, the present claims meet the written description requirement as articulated by the court in *Eli Lilly*.

The Synopsis of Written Description Guidelines published by the United States Patent and Trademark Office (the “Guidelines”) includes an example of a claim drawn to a protein defined by sequence (percent identity to a reference sequence) and function (ability to catalyze a particular reaction) and supported by a specification disclosing an assay for the specified function. The Guidelines state that such claims can meet the written description requirement. Here, the nucleic acid molecules encode polypeptide defined by sequence (percent identity a reference sequence, SEQ ID NO:2) and a function (phosphoglycerate mutase activity). These claims are supported by a specification disclosing an assay for the specified function. Thus, it is Applicants’ position that the present claims meet the written description requirement as articulated in the prevailing case law and consistent with the USPTO’s own guidelines.

In view of the forgoing, Applicants respectfully submit that the rejection based on the written description requirement of 35 U.S.C. §112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. §112, first paragraph (enablement)

The Examiner rejected previously pending claims 5, 6, 8 and 10 as allegedly failing to failing to meet the enablement requirement of 35 U.S.C. §112, first paragraph.

Given the teachings of the specification, one skilled in the art could make and use the claimed nucleic acids without undue experimentation because the specification teaches one skilled in the art how to identify nucleic acid molecules encoding biologically active polypeptides. The Court of Appeals for the Federal Circuit has identified eight factors that must be considered in determining whether undue experimentation would be required to practice a claimed invention: "(1) the quantity of experimentation necessary, (2) the amount and direction of guidance provided, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988).

With respect to the relative skill in the art, it is clear that the relative skill in art of generating variant polypeptides is very high. For example, those skilled in the art are aware of various random mutagenesis protocols can be used to create libraries of clones encoding variant polypeptides.

With respect to the guidance provided by the specification, the Examiner argues that specification does not provide sufficient guidance to enable one of ordinary skill in that art to identify functional polypeptides within the scope of the claims.

Applicants disagree with the Examiner's assertion that the specification does not provide sufficient guidance regarding which regions of the polypeptide are important for activity and which amino acid substitutions are likely to be functional. The specification provides the amino acid sequences of two different phosphoglycerate mutase proteins (*C. elegans* and *M. incognita*). Figure 3 of the specification provides an alignment of amino acid sequence of these two proteins.

The sequence alignment of Figure 3 provides ample guidance to those of ordinary skill in art in creating functional polypeptides within the claims. Of course, in many case it is desirable to test the proteins for functional activity.

With respect to the absence or presence of working examples, the specification provides a working example of a *M. incognita* phosphoglycerate mutase

Regarding the breadth of the claims, it is Applicants' position that the claims are not excessively broad encompassing as they do nucleic acid molecules encoding polypeptides having at least 80% identity to a reference polypeptide (SEQ ID NO:2).

With respect to predictability, although it cannot always be predicted whether a given amino acid change will alter function, it is generally understood, despite some exceptions, that certain types of variants, e.g., those involving conservative amino acid substitutions are more likely to retain function. Moreover, the sequence alignment provided in Figure 3 of the application provides information that allows one to more predictably select functional polypeptides within the claims.

With respect to the amount of experimentation required, the guidance regarding conserved residues combined with the assays for phosphoglycerate mutase activity provided in the specification permit one to make and use the claimed invention without undue experimentation.

Consideration of the *Wands* factors leads to the conclusion that the specification enables one of ordinary skill in the art to make and to use the invention.

In view of the forgoing, Applicants respectfully request that the enablement rejections under 35 U.S.C. §112, first paragraph be withdrawn.

Applicant : Andrew P. Klock et al.
Serial No. : 10/082,894
Filed : February 26, 2002.
Page : 9 of 9

Attorney's Docket No.: 12557-003001 / PGM

Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 2/12/14

John W. Doremus ^{Reg. # 29,166}
Anita L. Meiklejohn, Ph.D.
Reg. No. 35,283

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

20753717.doc